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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/522,004

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Kenneth D Rice

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10/28/2008

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EXAMINER

MURRAY, JEFFREY H

ART UNIT

PAPER NUMBER

1624

MAIL DATE

DELIVERY MODE

10/28/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/522,004	Applicant(s) RICE ET AL.	
	Examiner JEFFREY H. MURRAY	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 June 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) 126-136 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 67,69,71,73,76,77,79,81-84,86-92,94-99,113,114,116-120,137-150,152 and 155 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Continuation of Disposition of Claims: Claims pending in the application are 67,69,71,73,76,77,79,81-84,86-92,94-99,113,114,116-120,126-150,152 and 155.

DETAILED ACTION

Status of Claims

1. Claims 67, 69, 71, 73, 76, 77, 79, 81-84, 86-92, 94-99, 113, 114, 116-120, 137-150, 152 and 155 are pending in this application. Claims 1-66, 68, 70, 72, 74, 75, 78, 80, 85, 93, 100-112, 115, 121-125, 151, 153 and 154 have been cancelled. This action is in response to the applicants' amendment after a non-final action and reply filed on June 27, 2008.

Withdrawn Rejections/Objections:

2. Applicant is notified that any outstanding rejection/objection that is not expressly maintained in this office action has been withdrawn or rendered moot in view of applicant's amendments and/or remarks.

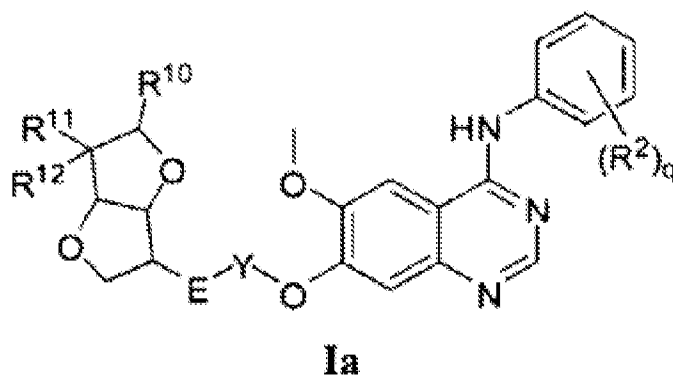
Claim Objections

3. Claims 79, 84, 89, 113-120, 140, 152 and 155 are objected to because of the following informalities:

Claims 79, 84, 89, 113-120, 140, 152 and 155 are objected to for containing non-elected subject matter within the claims. Appropriate correction is required.

Election/Restrictions

4. The Applicants have argued that no groups exist in the restriction requirement for any compounds of Formula Ia. Examiner disagrees. Formula Ia is as follows:



These compounds would clearly fall under Group V, X, or XV, based on the E and Y groups of the current restriction requirement. To avoid confusion concerning the ring systems that qualify under the M¹M²M³M⁴ group, the restriction is amended to read “heterocyclic ring systems” for each group in place of “heterocyclic ring” so that any bicyclic bridged ring system with at least 7 atoms and a nitrogen atom in the ring qualifies under Group VI of the restriction requirement. The restriction is still deemed proper and therefore remains **FINAL**.

5. Applicants have requested clarification concerning two issues. First, applicants have noted that the examiner incorrectly stated in group 9), in the enablement rejection on pages 4-5 of the previous action, a “5-methyl-2-azabicyclo[2.2.2]octane” group instead of a “8-methyl-8-azabicyclo[3.2.1]octane” group. Applicants are correct that this was an error and “8-methyl-8-azabicyclo[3.2.1]octane” was the intended group.

6. Second, examiner stated that applicants were enabled for a compound of Formula I whereby R¹ was a methoxy group. Applicants again were correct, examiner should have stated whereby R¹ is an alkyl group, therein forming a methoxy group. Examiner thanks applicants for pointing out these discrepancies.

Claim Rejections - 35 USC § 112, 1st Paragraph

7. Claims 67, 69, 71, 73, 76, 77, 79, 81-84, 86-92, 94-99, 113, 114, 116-120, 137-150, 152 and 155 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a compound, composition, stereoisomer, racemate, enantiomer, diastereomer or a pharmaceutically acceptable salt thereof where R¹ is an alkyl group; R² is a halogen, alkyl, haloalkyl, methoxy, aryloxy, or piperazinyl group; Z is a -NH- group; and M¹M²M³M⁴ is a -CH₂-bicyclic ring where the bicyclic ring is one of the following: 1) a 5-octahydrocyclopenta[c]pyrrole group; 2) a 3-hexahydro-1H-[1,4]oxazino[3,4-c][1,4]oxazine group; 3) a 3-hexahydro-1H-pyrrolo[2,1-c][1,4]oxazine group; 4) a 3-octahydro-1H-pyrido[1,2-a]pyrazin-1-one group; 5) a 3-hexahydropyrrolo[1,2-a]pyrazin-1(2H)-one group; 6) a 3-hexahydrothiazolo[4,3-c][1,4]oxazine group; 7) a 3-octahydro-1H-quinolizine group; and, 8) a 8-methyl-8-azabicyclo[3.2.1]octane group, does not reasonably provide enablement for any other residue groups or bicyclic heterocyclic groups other than those previously mentioned. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

8. Applicants have argued that the examiner examined claims in a manner that is counter to established USPTO practice. Applicants have argued that it is the duty of the examiner to prove the applicants have not shown how to make and use the invention without undue experimentation in a manner commensurate in scope with the claims. Examiner disagrees. The standard to be used is that of "one skilled in the art."

The question that must be asked is, "From the examples given by the applicants, would one ordinarily skilled in the art find the provided examples representative of the full scope of the claim(s) to synthesize compounds where $M^1M^2M^3M^4$ may be any 7-membered or greater heterocyclic ring system containing at least one nitrogen.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation. (*United States v. Teletronics Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based on a single factor, but rather a conclusion reached by weighing many factors (See *Ex parte Forman* 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). These factors were argued in the past action.

Within the specification, "specific operative embodiments or examples of the invention must be set forth. Examples and description should be of sufficient scope as to justify the scope of the claims. *Markush* claims must be provided with support in the disclosure for each member of the *Markush* group. Where the constitution and formula of a chemical compound is stated only as a probability or speculation, the disclosure is not sufficient to support claims identifying the compound by such composition or formula." See MPEP 608.01(p).

The compound core depicted with specific substituents represents a narrow subgenus for which applicant has provided sufficient guidance to make and use; however, this disclosure is not sufficient to allow extrapolation of the limited examples to enable the scope of the compounds instantly claimed or preventive agents. Applicant

has provided no working examples of any compositions where the compound of formula (1) did not contain the variables previously mentioned above in the present application.

There is no disagreement that the applicants have put forth examples of several compounds within the current specification, over 140 examples to be exact. However, of these examples, several do not encompass the invention claimed in the current application as it has been restricted. However, applicants have provided working examples of some enabled embodiments. The applicants presume that because examples have been shown that this is the final step and they are enabled. However, this is not the case. Applicants have not discussed the second step in determining enablement. The second step in determining the scope of enablement of a claim or claims is to ask, "Are the enabled embodiments representative of the full scope of the claim?" It would seem acceptable for a chemist skilled in the art to determine that "if a chloro group was synthesized, then other halogen atoms, such as a fluoro or bromo group could be accomplished" or "if a dimethylamino group was synthesized, other alkyl amino groups could also be synthesized." So, to an extent, these examples do embody groups larger than just themselves, but to state that all of the groups presented in this application are embodied, to make the leap that applicants have made, because a select group of examples has been shown that any and all of the Markush groups would be enabled is not prudent. The aforementioned groups that are considered enabled certainly do not embody or encompass the groups that have not been enabled. The arguments have not been found persuasive. The rejection is hereby maintained.

MPEP §2164.01 (a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here that Applicant is not enabled for making these compounds or compositions.

Claim Rejections - 35 USC § 112, 2nd Paragraph

9. The scope of "heterocyclyl" still requires clarification. The explanation involving monofused carbocycles which may appear to include benzo rings fused to heterocyclic rings was just one example. Applicants have not defined this term with reasonable clarity. The terms are defined with non-limiting examples making them impossible to pin down. For example, when one states C₁-C₄ alkyl, there are a small finite number of possibilities that exist in that set. One ordinarily skilled in the art realizes and understands this. However when one states, "heterocyclyl" and then provides a list of well over 50 examples and states the list is non-limiting, how can this be considered definite? One skilled in the art could instantly envision well over one hundred ring systems that qualify under this broad, vague definition. Does the applicant wish to claim a thiophene or a pyrazolopyrimidine? Applicant must narrow such broad terminology by either eliminating such a broad definition or by inserting the specific ring systems they wish to cover into the claim themselves. These arguments also apply to definitions within the specification which contain these terms, such as "heterocyclylalkyl."

The arguments have not been found persuasive. The rejection is maintained. No new matter permitted. Appropriate correction is required.

Conclusion

10. Claims 67, 69, 71, 73, 76, 77, 79, 81-84, 86-92, 94-99, 113, 114, 116-120, 137-150, 152 and 155 are rejected.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey H. Murray whose telephone number is 571-272-9023. The examiner can normally be reached on Mon.-Thurs. 7:30-6pm EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1624

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey H Murray/
Patent Examiner, Art Unit 1624

**/James O. Wilson/
Supervisory Patent Examiner, Art Unit 1624**